GenCore version 4.5

OM protein - protein search, using sw model

Run on: September 27, 2001, 16:29:47 ; Search time 34.59 Seconds
(without alignments)
557.341 Million cell updates/sec

Title: US-09-483-543A-8
Perfect score: 1693
Sequence: 1 KRGQAGNFDSEERSSWYWGR.....QQNPDEDFSGCGXGLEVLFQ 318

Scoring table: BLOSUM62
Gapop 10.0 , Gapext 0.5

Searched: 412676 seqs, 60623988 residues

Total number of hits satisfying chosen parameters: 412676

Minimum DB seq length: 0
Maximum DB seq length: 2000000000

Post-processing: Minimum Match 0%
Maximum Match 100%
Listing first 45 summaries

Database : A_Geneseq_0601:*
1: /SIDS8/gcgdata/geneseq/geneseqp/AA1980.DAT:*
2: /SIDS8/gcgdata/geneseq/geneseqp/AA1981.DAT:*
3: /SIDS8/gcgdata/geneseq/geneseqp/AA1982.DAT:*
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8: /SIDS8/gcgdata/geneseq/geneseqp/AA1987.DAT:*
9: /SIDS8/gcgdata/geneseq/geneseqp/AA1988.DAT:*
10: /SIDS8/gcgdata/geneseq/geneseqp/AA1989.DAT:*
11: /SIDS8/gcgdata/geneseq/geneseqp/AA1990.DAT:*
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19: /SIDS8/gcgdata/geneseq/geneseqp/AA1998.DAT:*
20: /SIDS8/gcgdata/geneseq/geneseqp/AA1999.DAT:*
21: /SIDS8/gcgdata/geneseq/geneseqp/AA2000.DAT:*
22: /SIDS8/gcgdata/geneseq/geneseqp/AA2001.DAT:*

Pred. No. is the number of results predicted by chance to have a score greater than or equal to the score of the result being printed, and is derived by analysis of the total score distribution.

SUMMARIES

Result No.	Score	% Query Match	Length	DB	ID	Description
1	1605	94.8	304	17	AAW05409	Mouse Crk protein.
2	1129	66.7	256	16	AAR85919	Human GRB-3. Homo
3	917.5	54.2	303	19	AAW42071	Human Crk-like pro
4	913.5	54.0	303	17	AAR77439	Mouse CRKL protein
5	321	19.0	79	19	AAW54313	NH2-terminal c-CRK
6	257	15.2	50	21	AAB12071	SH3 domain from v-
7	257	15.2	217	18	AAW18063	Growth factor rece
8	224	13.2	217	16	AAR85918	Human GRB-2. Homo
9	224	13.2	217	18	AAW14004	Human GRB2. Homo
10	224	13.2	217	19	AAW42070	Growth factor rece
11	222	13.1	217	16	AAR84636	Grb2 protein. Hom
12	210	12.4	317	13	AAR26061	Growth Factor Rece
13	177	10.5	1290	17	AAR90583	Phospholipase C-ga
14	174	10.3	845	21	AAY49419	PKA substrate, Vav
15	172.5	10.2	797	20	AAY27125	Amino acid sequenc
16	167	9.9	844	13	AAR25671	Mouse vav proto on
17	159.5	9.4	287	20	AAY22236	Human KDR signal t
18	159.5	9.4	847	20	AAY22237	Human KDR signal t
19	158.5	9.4	330	21	AAY97991	Human Grf40, a sig
20	158	9.3	1215	20	AAY32156	Human SH3D1A prote
21	158	9.3	1220	20	AAY32155	Human SH3D1A prote
22	157	9.3	462	17	AAW05395	Human SH3P17 prote
23	157	9.3	509	17	AAW05399	Human clone 65 pro
24	157	9.3	641	20	AAY32158	Human SH3D1A prote
25	157	9.3	1144	20	AAY32154	Human SH3D1A prote
26	156.5	9.2	330	21	AAY69388	Amino acid sequenc
27	154.5	9.1	1715	21	AAY57449	Mouse Esel1L protei
28	152	9.0	1214	21	AAY57444	Mouse Esel protein
29	151.5	8.9	330	19	AAW76830	Human GRBP protein
30	149	8.8	464	18	AAW26496	CD2 associated int
31	149	8.8	464	18	AAW25116	CD2-associated int
32	149	8.8	464	20	AAW80420	CD2 associated int
33	149	8.8	464	22	AAB66391	Human CD2 associat
34	147.5	8.7	788	17	AAW05393	Mouse SH3P12 prote
35	147	8.7	1197	21	AAY57445	Mouse Ese2 protein
36	147	8.7	1658	21	AAY57450	Mouse Ese2L protei
37	144.5	8.5	516	15	AAR46685	Peptide P9 inhibit
38	144.5	8.5	1047	11	AAR06328	Sequence of full l
39	144.5	8.5	1047	12	AAR11137	GAP6 encoded by la
40	144.5	8.5	1047	13	AAR25336	Lambda clone 101 p
41	143.5	8.5	870	15	AAR59924	Human GAP protein.
42	141.5	8.4	1683	21	AAY71160	Rat phosphodiester
43	141	8.3	553	18	AAW26495	CD2 associated int
44	141	8.3	553	18	AAW25115	CD2-associated int
45	141	8.3	553	20	AAW80419	CD2 associated int

ALIGNMENTS

RESULT 1
AAW05409
ID AAW05409 standard; Protein; 304 AA.
XX
AC AAW05409;
XX
DT 23-FEB-1998 (first entry)
XX
DE Mouse Crk protein.
XX
KW Src-homology region 3 domain; human; mouse; SH3 domain; cell growth;
KW cellular signalling element; cellular structural element; malignancy;
KW protein identification; functional domain; protein screening;
KW cellular signal transduction process.
XX
OS Mus musculus.
XX
FH Key Location/Qualifiers
FT Misc-difference 167
FT /note= "encoded by GAC"
FT Misc-difference 168
FT /note= "encoded by GAG"
XX
PN WO9631625-A1.
XX
PD 10-OCT-1996.
XX
PF 04-APR-1996; 96WO-US04454.
XX
PR 03-APR-1996; 96US-0630915.
PR 07-APR-1995; 95US-0417872.
XX
PA (CYTO-) CYTOGEN CORP.
PA (UYNC-) UNIV NORTH CAROLINA.

```
XX
PI   Fowlkes DM,  Hoffman N,  Kay BK,  Mcconnell SJ,  Sparks AB;
XX
DR   WPI; 1996-465045/46.
DR   N-PSDB; AAT39808.
XX
PT   Identifying polypeptide(s) having specific functional domain (esp.
PT   SH3 domain) - comprises detecting selective binding to recognition
PT   unit, regardless of sequence homology
XX
PS   Claim 102; Fig 41; 174pp; English.
XX
CC   AAW05405-W05411 represent human and mouse Src-homology region 3 (SH3)
CC   domain containing proteins that can be used in the method of the
CC   invention. SH3 domain containing proteins play a role in signalling and
CC   structural elements of cells. The method of the invention is for
CC   identifying polypeptides containing functional domains of interest
CC   (especially SH3 domains). The method comprises contacting a multivalent
CC   recognition unit (RU) complex with a number of peptides and identifying
CC   polypeptides having a selective binding affinity for the RU complex. The
CC   method is based on functional similarities and does not rely on sequence
CC   similarities. Prior methods only gave limited success for identifying
CC   proteins which contain an SH3 domain due to the minimal sequence
CC   homology among known SH3 proteins. It has been found that small peptide
CC   RUs in multivalent form have reduced specificity for a given functional
CC   domain compared to monomer RUs. Multivalent RU complexes are particularly
CC   suited to screening for polypeptides containing functional domains that
CC   are similar to, but not identical in sequence to, the original target
CC   functional domain. The new method enables proteins having a common
CC   function to be identified. Identification of novel SH3 proteins will be
CC   useful for a better understanding of cell growth, malignancy, signal
CC   transduction processes, etc. New candidate drugs can be identified, and
CC   their specificities (e.g. pharmacological activities) can be assessed
CC   using the method of the invention.
XX
SQ   Sequence   304 AA;

  Query Match             94.8%;  Score 1605;  DB 17;  Length 304;
  Best Local Similarity   99.7%;  Pred. No. 5.5e-135;
  Matches  302;  Conservative    0;  Mismatches    1;  Indels    0;  Gaps    0;

Qy       5 AGNFDSEERSSWYWGRLSRQEAVALLQGQRHGVFLVRDSSTSPGDYVLSVSENSRVSHYI 64
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2 agnfdseersswywgrlsrqeavallqgqrhgvflvrdsstspgdyvlsvsensrvshyi 61

Qy      65 INSSGPRPPVPPSPAQPPPGVSPSRLRIGDQEFDSLPALLEFYKIHYLDTTTLIEPVARS 124
           |||||||||||||||||||||||||| |||||||||||||||||||||||||||||||||
Db      62 inssgprppvppspaqpppgvspsrlrighqefdslpallefykihyldtttliepvars 121

Qy     125 RQGSGVILRQEEAEYVRALFDFNGNDEEDLPFKKGDILRIRDKPEEQWWNAEDSEGKRGM 184
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     122 rqgsgvilrqeeaeyvralfdfngndeedlpfkkgdilrirdkpeeqwwnaedsegkrgm 181

Qy     185 IPVPYVEKYRPASASVSALIGGNQEGSHPQPLGGPEPGPYAQPSVNTPLPNLQNGPIYAR 244
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     182 ipvpyvekyrpasasvsaliggnqegshpqplggpepgpyaqpsvntplpnlqngpiyar 241

Qy     245 VIQKRVPNAYDKTALALEVGELVKVTKINVSGQWEGECNGKRGHFPFTHVRLLDQQNPDE 304
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     242 viqkrvpnaydktalalevgelvkvtkinvsgqwegecngkrghfpfthvrlldqqnpde 301

Qy     305 DFS 307
           |||
Db     302 dfs 304


RESULT   2
AAR85919
ID   AAR85919 standard; Protein; 256 AA.
XX
AC   AAR85919;
XX
DT   16-MAY-1996  (first entry)
XX
DE   Human GRB-3.
XX
KW   GRB-3; growth factor receptor bound; tyrosine kinase; regulation;
KW   cell growth; cellular metabolism; screening; signal transduction;
KW   cancer; diabetes; CORT technique; cloning of receptor targets.
XX
OS   Homo sapiens.
XX
PN   WO9524426-A1.
XX
PD   14-SEP-1995.
XX
PF   13-MAR-1995;   95WO-US03385.
XX
PR   11-MAR-1994;   94US-0208887.
XX
PA   (UYNY ) UNIV NEW YORK STATE.
XX
PI   Margolis BL,  Schlessinger J,  Skolnik EY;
XX
DR   WPI; 1995-328235/42.
DR   N-PSDB; AAT07168.
XX
PT   DNA encoding tyrosine kinase-binding proteins - used to screen
PT   agents capable of modulating cell growth or cellular metabolism
XX
PS   Disclosure; Fig 34A-C; 215pp; English.
XX
CC   Using a new cloning technique, CORT (cloning of receptor targets)
CC   several new tyrosine kinase (TK) binding proteins were isolated. Growth
CC   factor receptor bound proteins GRB-1,GRB-2, GRB-3, GRB-4, GRB-7 and
CC   GRB-10 were isolated using this method. This sequence represents GRB-3.
CC   The proteins bind to a tyrosine-phosphorylated domain of a eukaryotic
CC   TK. GRB proteins can be used for screening agents which are capable
CC   of modulating cell growth that occurs via signal transduction through
CC   TKs. Such agents can be used to prevent or inhibit cell growth or to
CC   counteract tumour development. GRB proteins are also useful for
CC   identifying susceptibility to diseases asociated with alterations in
CC   cellular metabolism mediated by TK pathways e.g. cancer and diabetes.
XX
SQ   Sequence   256 AA;

  Query Match             66.7%;  Score 1129;  DB 16;  Length 256;
  Best Local Similarity   98.2%;  Pred. No. 1.1e-92;
  Matches  215;  Conservative    0;  Mismatches    4;  Indels    0;  Gaps    0;

Qy       5 AGNFDSEERSSWYWGRLSRQEAVALLQGQRHGVFLVRDSSTSPGDYVLSVSENSRVSHYI 64
           |||||||||||||||||||||||||||| ||||||||||||||||||||||||||||||
Db      33 agnfdseersswywgrlsrqeavallqgqrdgvflvrdsstspgdyvlsvsensrvshyi 92

Qy      65 INSSGPRPPVPPSPAQPPPGVSPSRLRIGDQEFDSLPALLEFYKIHYLDTTTLIEPVARS 124
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      93 inssgprppvppspaqpppgvspsrlrigdqefdslpallefykihyldtttliepvars 152

Qy     125 RQGSGVILRQEEAEYVRALFDFNGNDEEDLPFKKGDILRIRDKPEEQWWNAEDSEGKRGM 184
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     153 rqgsgvilrqeeaeyvralfdfngndeedlpfkkgdilrirdkpeeqwwnaedsegkrgm 212

Qy     185 IPVPYVEKYRPASASVSALIGGNQEGSHPQPLGGPEPGP 223
           |||||||||||||||||||||||||||||||   ||
Db     213 ipvpyvekyrpasasvsaliggnqegshpqplggrslgp 251


RESULT   3
AAW42071
ID   AAW42071 standard; Protein; 303 AA.
XX
AC   AAW42071;
XX
DT   04-JUN-1998  (first entry)
```

```
XX
DE   Human Crk-like protein Crkl.
XX
KW   Crk-like; Crkl; CML; translation initiation site; bcr-abl;
KW   chronic myelogenous leukaemia; cancer.
XX
OS   Homo sapiens.
XX
FH   Key             Location/Qualifiers
FT   Domain          14..64
FT                   /label= SH2
FT   Domain          78..101
FT                   /label= SH2'
FT   Domain          131..179
FT                   /label= SH3
FT   Domain          238..290
FT                   /label= SH3
FT                   /note= "This domain is designated SH4 in the disclosure"
XX
PN   WO9801547-A1.
XX
PD   15-JAN-1998.
XX
PF   08-JUL-1997;   97WO-US10101.
XX
PR   08-JUL-1996;   96US-0679437.
XX
PA   (TEXA ) UNIV TEXAS SYSTEM.
XX
PI   Arlinghaus RB,  Lopez-Berestein G,  Tari AM;
XX
DR   WPI; 1998-110229/10.
DR   N-PSDB; AAV09214.
XX
PT   Use of anti-sense oligo:nucleotide(s) to Grb2 or Crkl nucleic acids
PT   - for inhibiting growth of cancer cells in treatment of cancers,
PT   particularly chronic myelogenous leukaemia
XX
PS   Disclosure; Fig 5; 47pp; English.
XX
CC   This is the sequence of human Crkl. Translation of Crkl cDNA can be
CC   inhibited by oligonucleotides of specific composition that
CC   hybridise to its translation initiation site. The oligonucleotide
CC   compositions can be used for treating, particularly chronic
CC   myelogenous leukaemia (CML). See AAV09216.
XX
SQ   Sequence   303 AA;


  Query Match             54.2%;  Score 917.5;  DB 19;  Length 303;
  Best Local Similarity   56.6%;  Pred. No. 9.1e-74;
  Matches  185;  Conservative   33;  Mismatches   56;  Indels   53;  Gaps    6;

Qy       5 AGNFDSEERSSWYWGRLSRQEAVALLQGQRHGVFLVRDSSTSPGDYVLSVSENSRVSHYI 64
           :  ||| :||:|| | :|||||   |||||||:|||||||| ||||||||||||||||||
Db       3 sarfdssdrsawymgpvsrqeaqtrlqgqrhgmflvrdsstcpgdyvlsvsensrvshyi 62

Qy      65 INSSGPRPPVPPSPAQPPPGVSPSRLRIGDQEFDSLPALLEFYKIHYLDTTTLIEPVAR- 123
           |||   |                 | :||||||| ||||||||||||||||||||||  |
Db      63 inslpnr-----------------rfkigdqefdhlpallefykihyldtttliepapry 105

Qy     124 ------SRQGSGVILRQEEAEYVRALFDFNGNDEEDLPFKKGDILRIRDKPEEQWWNAED 177
                 |     :   ::  |||| |:|| ||| ||||||||:|| | :|||||||:| :
Db     106 psppmgsvsapnlptaednleyvrtlydfpgndaedlpfkkgeilviiekpeeqwwsarn 165

Qy     178 SEGKRGMIPVPYVEKYRPASASVSALIGGNQEGSH----PQPLGGPEPG-PYAQPSVN-- 230
            :|: ||||||||||          |:  :  | |        | |||   ||||
Db     166 kdgrvgmipvpyvek----------lvrssphgkhgnrnsnsygipepahayaqpqtttp 215

Qy     231 ------------TPLPNLQNGPIYARVIQKRVPNAYDKTALALEVGELVKVTKINVSGQW 278
                       ||||: ||||::|: |||||| ||||||||||||::||||::|::|||
Db     216 lpavsgspgaaitplpstqngpvfakaiqkrvpcaydktalalevgdivkvtrmningqw 275

Qy     279 EGECNGKRGHFPFTHVRLLDQQNPDED 305
           ||| ||::| |||||:: | |||||:
Db     276 egevngrkglfpfthvkifdpqnpden 302


RESULT   4
AAR77439
ID   AAR77439 standard; Protein; 303 AA.
XX
AC   AAR77439;
XX
DT   21-JUL-1996  (first entry)
XX
DE   Mouse CRKL protein.
XX
KW   Mouse CRKL protein; tyrosine phosphorylation; diagnosis;
KW   chronic myelogenous leukaemia; acute lymphoblastic leukaemia;
KW   Philadelphia chromosome; BCL; ABL; treatment.
XX
OS   Mus musculus.
XX
FH   Key             Location/Qualifiers
FT   Binding-site
FT   Domain          9..103
FT                   /note= "SH2 domain""
FT   Domain          131..179
FT                   /note= "N-terminal SH3 domain"
FT   Modified-site   193..210
FT                   /note= "tyrosine phosphorylation site"
FT   Domain          238..290
FT                   /note= "C-terminal SH3 domain"
XX
PN   WO9531545-A2.
XX
PD   23-NOV-1995.
XX
PF   12-MAY-1995;   95WO-US05957.
XX
PR   13-MAY-1994;   94US-0242513.
XX
PA   (CHIL-) CHILDRENS HOSPITAL LOS ANGELES.
XX
PI   Groffen JH,  Heisterkamp NC,  Ten Hoeve J;
XX
DR   WPI; 1996-010931/01.
DR   N-PSDB; AAT04144.
XX
PT   Diagnosis of tyrosine phosphorylated CRKL protein cancers - by
PT   detecting increased level of CRKL protein or CRKL binding protein,
PT   also compsns. for treating chronic myelogenous leukaemia.
XX
PS   Claim 37; Fig 10b; 74pp; English.
XX
CC   The mouse CRKL protein may be used in the diagnosis of Philadelphia
CC   chromosome-positive leukaemias.  For example, since CRKL is clearly
CC   tyrosine-phosphorylated in chronic myelogenous leukaemia and
CC   Philadelphia chromosome (Ph)-positive acute lymphoblastic leukaemia
CC   patients expressing the BCR/ABL protein, but not in BCR-ABL-negative
CC   peripheral blood cells, tyrosine-phosphorylation of CRKL may be used
CC   as a diagnostic indicator for BCL/ABL activity in Ph-positive
CC   leukaemia.  Thus, overexpression of tyrosine-phosphorylated CRKL
CC   protein, or an increase in protein, gene copy number or mRNA is
CC   indicative of Ph-positive leukaemia.  Fragments of the CRKL protein
CC   may also be used in the treatment of individuals with cancers
CC   arising from cells which express the CRKL protein by inhibition of
CC   the synthesis or activity of the CRKL protein.
XX
SQ   Sequence   303 AA;


  Query Match             54.0%;  Score 913.5;  DB 17;  Length 303;
  Best Local Similarity   56.0%;  Pred. No. 2.1e-73;
  Matches  183;  Conservative   35;  Mismatches   56;  Indels   53;  Gaps    6;
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```
Qy       5 AGNFDSEERSSWYWGRLSRQEAVALLQGQRHGVFLVRDSSTSPGDYVLSVSENSRVSHYI 64
           :  ||| :||:|| | ::|||   |||||||:|||||||| ||||||||||||||||||
Db       3 sarfdssdrsawymgpvtrqeaqtrlqggrhgmflvrdsstcpgdyvlsvsensrvshyi 62

Qy      65 INSSGPRPPVPPSPAQPPPGVSPSRLRIGDQEFDSLPALLEFYKIHYLDTTTLIEPVAR- 123
           |||   |                | :||||||| ||||||||||||||||||||  |
Db      63 inslpnr-----------------rfkigdqefdhlpallefykihyldtttliepapry 105

Qy     124 ------SRQGSGVILRQEEAEYVRALFDFNGNDEEDLPFKKGDILRIRDKPEEQWWNAED 177
                |     :   :|  |||| |:|| ||| |||||||::| | :|||||||:| :
Db     106 psppvgsvsapnlptaeenleyvrtlydfpgndaedlpfkkgellviiekpeeqwwsarn 165

Qy     178 SEGKRGMIPVPYVEKYRPASASVSALIGGNQEGSH----PQPLGGPEPG-PYAQPSVNTP 232
            :|: ||||||||||          |:  :  | |        | |||   ||||   ||
Db     166 kdgrvgmipvpyvek----------lvrssphgkhgnrnsnsygipepahayaqpqtttp 215

Qy     233 LPNL-------------QNGPIYARVIQKRVPNAYDKTALALEVGELVKVTKINVSGQW 278
           || :              ||||::|: |||||| ||||||||||||::||||::|::|||
Db     216 lptvastpgaainplpstqngpvfakaiqkrvpcaydktalalevgdivkvtrmningqw 275

Qy     279 EGECNGKRGHFPFTHVRLLDQQNPDED 305
           ||| ||::| |||||:: | ||||::
Db     276 egevngrkglfpfthvkifdpqnpddn 302
```

RESULT 5
AAW54313
ID AAW54313 standard; peptide; 79 AA.
XX
AC AAW54313;
XX
DT 30-JUL-1998 (first entry)
XX
DE NH2-terminal c-CRK SH3 domain derivative.
XX
KW Non-specific interaction; ligand; identification; catalyst; therapeutic;
KW diagnostic.
XX
OS Synthetic.
XX
PN WO9811436-A1.
XX
PD 19-MAR-1998.
XX
PF 15-SEP-1997; 97WO-US16424.
XX
PR 13-SEP-1996; 96US-0714792.
XX
PA (NECA-) NETHERLANDS CANCER INST.
PA (WHED) WHITEHEAD INST BIOMEDICAL RES.
XX
PI Kim PS, Schumacher ANM;
XX
DR WPI; 1998-207532/18.
XX
PT Enhancing the concentration of ligand for target molecule - using
PT library of potential ligands with binding pair member and target
PT molecule with second binding pair member
XX
PS Example 2; Page 27; 38pp; English.
XX
CC The peptides AAW54313-W54314 were used in the demonstration of the
CC effect of a non-specific interaction on the identification of ligands
CC for targets of interest. The identifcation of ligands or catalysts from
CC a library can be used for detecting ligands such as proteins and
CC oligonucleotides. The ligands obtained can be used as drugs and
CC reagents for therapeutic and diagnostic purposes and as lead molecules
CC for drug design. The catalysts obtained can be used e.g. to produce
CC pharmaceuticals, materials such as plastics and other polymers, and
CC other products such as food products, detergents and other cleansers and
CC oral hygiene products (e.g. toothpastes, mouthwashes).
XX
SQ Sequence 79 AA;

Query Match 19.0%; Score 321; DB 19; Length 79;
Best Local Similarity 96.7%; Pred. No. 2e-21;
Matches 59; Conservative 0; Mismatches 2; Indels 0; Gaps 0;

```
Qy     137 AEYVRALFDFNGNDEEDLPFKKGDILRIRDKPEEQWWNAEDSEGKRGMIPVPYVEKYRPA 196
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      12 aeyvralfdfngndeedlpfkkgdilrirdkpeeqwwnaedsegkrgmipvpyvekyrgg 71

Qy     197 S 197
           |
Db      72 s 72
```

RESULT 6
AAB12071
ID AAB12071 standard; Peptide; 50 AA.
XX
AC AAB12071;
XX
DT 17-JAN-2001 (first entry)
XX
DE SH3 domain from v-crk.
XX
KW Rb-interacting zinc finger; RIZ; retinoblastoma; heart disease;
KW cell proliferation; cell differentiation; tissue repair;
KW transcription regulator; breast cancer; gene therapy; melanoma;
KW neuroblastoma; leukaemia; Parkinson's disease; Huntingdon's disease;
KW Alzheimer's disease; paralysis; motor neurone disorder;
KW SH3 domain.
XX
OS Unidentified.
XX
PN US6069231-A.
XX
PD 30-MAY-2000.
XX
PF 18-AUG-1995; 95US-0516859.
XX
PR 18-AUG-1994; 94US-0292683.
PR 06-MAR-1995; 95US-0399411.
XX
PA (LJOL-) LA JOLLA CANCER RES FOUND.
XX
PI Huang S;
XX
DR WPI; 2000-410879/35.
XX
PT New PR domain peptides comprising amino acid sequences from, for
PT example retinoblastoma-interacting zinc finger, or egl-43 proteins, for
PT regulating gene transcription and controlling cell proliferation and
PT differentiation -
XX
PS Disclosure; Fig 2; 91pp; English.
XX
CC The present sequence is the SH3 domain from v-crk protein. A SH3
CC domain is also found in rat RIZ (AAB12028). RIZ is retinoblastoma
CC (Rb)-interacting zinc finger protein. RIZ is a nuclear phosphoprotein
CC that acts as a cell differentiation factor. RIZ can modulate cell growth
CC by binding to Rb protein, which is involved in regulating cell
CC proliferation. In addition, RIZ can act to regulate transcription. RIZ
CC functions to maintain cells in the G1 phase of the cell cycle, by
CC interacting with Rb through the cr2 domain of RIZ. Rat RIZ protein
CC contains a number of GTPase motifs (see AAB12037 to AAB12056 and AAB12099
CC to AAB12104). RIZ protein is a PR domain protein and is present primarily
CC in the cell nucleus. RIZ gene mutations may be implicated in various
CC cancers such as melanoma, neuroblastoma, leukaemia and breast cancer, and
CC so the RIZ gene may be used in gene therapy for these disorders. Since
CC RIZ protein is implicated in cell cycle arrest, inhibition of RIZ
CC activity may be useful in neurodegenerative disorder therapy e.g. for
CC Parkinson's, Huntingdon's or Alzheimer's disease, paralysis or motor

```
CC   neurone disorders, or cardiac disorders e.g. heart disease, where the
CC   ability to induce neural/ cardiac tissue proliferation would be useful.
CC   The present sequence was used for sequence homology comparison.
XX
SQ   Sequence   50 AA;


  Query Match             15.2%;  Score 257;  DB 21;  Length 50;
  Best Local Similarity   90.0%;  Pred. No. 5.4e-16;
  Matches   45;  Conservative    3;  Mismatches    2;  Indels    0;  Gaps    0;

Qy    142 ALFDFNGNDEEDLPFKKGDILRIRDKPEEQWWNAEDSEGKRGMIPVPYVE 191
          ||||| |||:|||||||||||:|||||||||||||| :|||||||||||
Db      1 alfdfkgnddedlpfkkgdilkirdkpeeqwwnaedmdgkrgmipvpyve 50


RESULT   7
AAW18063
ID   AAW18063 standard; Protein; 217 AA.
XX
AC   AAW18063;
XX
DT   06-DEC-1997  (first entry)
XX
DE   Growth factor receptor-binding protein 2 homologue Grb2-1.
XX
KW   Growth factor receptor-binding protein 2 homologue; Grb2-1; human;
KW   signal transduction; antagonist; antisense; immunosuppressive;
KW   autoimmune disease; transplant rejection; agonist; HIV; infection;
KW   cancer; diagnosis; gene therapy.
XX
OS   Homo sapiens.
XX
PN   WO9720573-A1.
XX
PD   12-JUN-1997.
XX
PF   04-DEC-1995;   95WO-US15883.
XX
PR   04-DEC-1995;   95WO-US15883.
XX
PA   (HUMA-) HUMAN GENOME SCI INC.
PA   (JOSL-) JOSLIN DIABETES CENT INC.
PA   (SMIK ) SMITHKLINE BEECHAM CORP.
XX
PI   Dunnington D,  Ni J,  Shoelson SE;
XX
DR   WPI; 1997-319539/29.
DR   N-PSDB; AAT67275.
XX
PT   Growth factor receptor-binding protein 2 homologue and related DNA -
PT   used to develop products for diagnosis and therapy of, e.g.
PT   autoimmune diseases, transplant rejection, HIV infection or cancer
XX
PS   Claim 4; Page 38-39; 57pp; English.
XX
CC   This polypeptide comprises a human growth factor receptor-binding
CC   protein 2 homologue, Grb2-1 (AAW18063), that exhibits T-cell
CC   specificity.  Its amino acid sequence was deduced from a cDNA
CC   sequence (AAT67275) originally derived from a human tonsil cDNA
CC   library.  It shows 58% identity with the human Grb2 amino acid
CC   sequence.  Methods are claimed for producing pure human Grb2-1
CC   protein in a recombinant host cell, for treating conditions related
CC   to insufficient Grb2-1 protein function, and for identifying
CC   compounds that modulate Grb2-1 activity, such as substances that
CC   modulate the ras pathway in T-lymphocytes by affecting the binding
CC   of Grb2-1 to the cell membrane.  Modulation of Grb2-1 function can
CC   be used to affect immune system function by affecting T-cell
CC   proliferation pathways.  Antagonists have immunosuppressive
CC   activities and can be used to treat and prevent autoimmune diseases
CC   and transplant rejection.  Agonists can be used to treat immune
CC   deficiency states such as HIV infection or cancer.
XX
SQ   Sequence   217 AA;


  Query Match             15.2%;  Score 257;  DB 18;  Length 217;
  Best Local Similarity   31.4%;  Pred. No. 3.8e-15;
  Matches   64;  Conservative   40;  Mismatches   54;  Indels   46;  Gaps    9;

Qy      2 RGCAG----NFDSEERSSWYWGRLSRQEAVALLQGQRH-GVFLVRDSSTSPGDYVLSVSE 56
            ||  |    |:   :   || ||:||| |  :|  : | | ||:|:|:| :|||:: :||:
Db     42 rgvegfipknyirvkphpwysgrisrqlaeeilmkrnhlgafliresesspgefsvsvny 101

Qy     57 NSRVSHYII--NSSGPRPPVPPSPAQPPPGVSPSRLRIGDQEFDSLPALLEFYKIHYLDT 114
            :| |: :   :||                  :  : :::|:|| |::||:     |
Db    102 gdqvqhfkvlreasg-----------------kyflweekfnslnelvdfyr-----t 137

Qy    115 TTLIEPVARSRQGSGVILRQEE-------AEYVRALFDFNGNDEEDLPFKKGDILRIRDK 167
          ||    :|: ||   : || ||       | : :| |||:  |   | |::|||: : ::
Db    138 tt----iakkrq---iflrdeepllkspgacfaqaqfdfsaqdpsqlsfrrgdiievler 190

Qy    168 PEEQWWNAEDSEGKRGMIPVPYVE 191
          |:  ||    | |: |  |  ||:
Db    191 pdphwwrgr-scgrvgffprsyvq 213


RESULT   8
AAR85918
ID   AAR85918 standard; Protein; 217 AA.
XX
AC   AAR85918;
XX
DT   16-MAY-1996  (first entry)
XX
DE   Human GRB-2.
XX
KW   GRB-2; growth factor receptor bound; tyrosine kinase; regulation;
KW   cell growth; cellular metabolism; screening; signal transduction;
KW   cancer; diabetes; CORT technique; cloning of receptor targets.
XX
OS   Homo sapiens.
XX
PN   WO9524426-A1.
XX
PD   14-SEP-1995.
XX
PF   13-MAR-1995;   95WO-US03385.
XX
PR   11-MAR-1994;   94US-0208887.
XX
PA   (UYNY ) UNIV NEW YORK STATE.
XX
PI   Margolis BL,  Schlessinger J,  Skolnik EY;
XX
DR   WPI; 1995-328235/42.
DR   N-PSDB; AAT07167.
XX
PT   DNA encoding tyrosine kinase-binding proteins - used to screen
PT   agents capable of modulating cell growth or cellular metabolism
XX
PS   Disclosure; Fig 26A-C; 215pp; English.
XX
CC   Using a new cloning technique, CORT (cloning of receptor targets)
CC   several new tyrosine kinase (TK) binding proteins were isolated. Growth
CC   factor receptor bound proteins GRB-1,GRB-2, GRB-3, GRB-4, GRB-7 and
CC   GRB-10 were isolated using this method. This sequence represents GRB-2.
CC   The proteins bind to a tyrosine-phosphorylated domain of a eukaryotic
CC   TK. GRB proteins can be used for screening agents which are capable
CC   of modulating cell growth that occurs via signal transduction through
CC   TKs. Such agents can be used to prevent or inhibit cell growth or to
CC   counteract tumour development. GRB proteins are also useful for
CC   identifying susceptibility to diseases asociated with alterations in
CC   cellular metabolism mediated by TK pathways e.g. cancer and diabetes.
XX
SQ   Sequence   217 AA;
```

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  Query Match             13.2%;  Score 224;  DB 16;  Length 217;
  Best Local Similarity   27.9%;  Pred. No. 3.3e-12;
  Matches   53;  Conservative   44;  Mismatches   57;  Indels   36;  Gaps    7;

Qy       7 NFDSEERSSWYWGRLSRQEAVALLQGQRH-GVFLVRDSSTSPGDYVLSVSENSRVSHYII 65
           |:   :   |::|:: | :|  :|  ||| | ||:|:| ::|||: |||   : | |: :
Db      51 nyiemkphpwffgkiprakaeemlskqrhdgafliresesapgdfslsvkfgndvqhfkv 110

Qy      66 NSSGPRPPVPPSPAQPPPGVSPSRLRIGDQEFDSLPALLEFYKIHYLDTTTLIEPVARSR 125
             |                  :  :   :|:||  |:::::     :|:    |:|::
Db     111 lrdg----------------agkyflwvvkfnslnelvdyhr-----sts----vsrnq 144

Qy     126 QGSGVILRQ-----EEAEYVRALFDFNGNDEEDLPFKKGDILRIRDKPEEQWWNAEDSEG 180
           |   : ||      ::  ||:|||||:  :: :| |::|| : : |  :  ||      |
Db     145 q---iflrdieqvpqqptyvqalfdfdpqedgelgfrrgdfihvmdnsdpnwwkga-chg 200

Qy     181 KRGMIPVPYV 190
           : || |  ||
Db     201 qtgmfprnyv 210


RESULT   9
AAW14004
ID   AAW14004 standard; Protein; 217 AA.
XX
AC   AAW14004;
XX
DT   24-JUN-1997  (first entry)
XX
DE   Human GRB2.
XX
KW   SH2-containing inositol phosphatase; SHIP;
KW   inositol polyphosphate 5-phosphatase; src homology domain 2;
KW   SH2 domain; signal transduction; leukaemia; cancer; Grb2;
KW   epidermal growth factor receptor binding protein.
XX
OS   Homo sapiens.
XX
PN   WO9712039-A2.
XX
PD   03-APR-1997.
XX
PF   27-SEP-1996;   96WO-CA00655.
XX
PR   14-JUN-1996;   96US-0664962.
PR   27-SEP-1995;   95US-0006063.
PR   30-NOV-1995;   95US-0007788.
PR   09-APR-1996;   96US-0015217.
XX
PA   (KRYS/) KRYSTAL G.
XX
PI   Krystal G;
XX
DR   WPI; 1997-212898/19.
DR   N-PSDB; AAT60302.
XX
PT   Inositol polyphosphate-5-phosphatase having SH2 domain - useful for
PT   treating cancer and other conditions involving abnormal signalling
XX
PS   Disclosure; Page 47-48; 89pp; English.
XX
CC   Human epidermal growth factor receptor binding protein GRB2
CC   (AAW14003) is an src homology domain 3 (SH3) protein that is capable
CC   of binding to novel murine and human SHIP (SH2-containing inositol
CC   phosphatase) proteins (see also AAW14002-03).  It can be used in
CC   methods for identifying agonists and antagonists of SHIP.
XX
SQ   Sequence   217 AA;


  Query Match             13.2%;  Score 224;  DB 18;  Length 217;
  Best Local Similarity   27.9%;  Pred. No. 3.3e-12;
  Matches   53;  Conservative   44;  Mismatches   57;  Indels   36;  Gaps    7;

Qy       7 NFDSEERSSWYWGRLSRQEAVALLQGQRH-GVFLVRDSSTSPGDYVLSVSENSRVSHYII 65
           |:   :   |::|:: | :|  :|  ||| | ||:|:| ::|||: |||   : | |: :
Db      51 nyiemkphpwffgkiprakaeemlskqrhdgafliresesapgdfslsvkfgndvqhfkv 110

Qy      66 NSSGPRPPVPPSPAQPPPGVSPSRLRIGDQEFDSLPALLEFYKIHYLDTTTLIEPVARSR 125
             |                  :  :   :|:||  |:::::     :|:    |:|::
Db     111 lrdg----------------agkyflwvvkfnslnelvdyhr-----sts----vsrnq 144

Qy     126 QGSGVILRQ-----EEAEYVRALFDFNGNDEEDLPFKKGDILRIRDKPEEQWWNAEDSEG 180
           |   : ||      ::  ||:|||||:  :: :| |::|| : : |  :  ||      |
Db     145 q---iflrdieqvpqqptyvqalfdfdpqedgelgfrrgdfihvmdnsdpnwwkga-chg 200

Qy     181 KRGMIPVPYV 190
           : || |  ||
Db     201 qtgmfprnyv 210


RESULT  10
AAW42070
ID   AAW42070 standard; Protein; 217 AA.
XX
AC   AAW42070;
XX
DT   04-JUN-1998  (first entry)
XX
DE   Growth factor receptor-bound protein 2.
XX
KW   Growth factor receptor-bound protein 2; Grb-2; CML; bcr-abl;
KW   translation initiation site; chronic myelogenous leukaemia; cancer.
XX
OS   Homo sapiens.
XX
FH   Key             Location/Qualifiers
FT   Domain          5..54
FT                   /label= SH3
FT   Domain          60..158
FT                   /label= SH2
FT   Domain          163..208
FT                   /label= SH3
XX
PN   WO9801547-A1.
XX
PD   15-JAN-1998.
XX
PF   08-JUL-1997;   97WO-US10101.
XX
PR   08-JUL-1996;   96US-0679437.
XX
PA   (TEXA ) UNIV TEXAS SYSTEM.
XX
PI   Arlinghaus RB,  Lopez-Berestein G,  Tari AM;
XX
DR   WPI; 1998-110229/10.
DR   N-PSDB; AAV09213.
XX
PT   Use of anti-sense oligo:nucleotide(s) to Grb2 or Crkl nucleic acids
PT   - for inhibiting growth of cancer cells in treatment of cancers,
PT   particularly chronic myelogenous leukaemia
XX
PS   Disclosure; Fig 4; 47pp; English.
XX
CC   This is a polypeptide sequence of Grb-2. Translation of Grb-2 cDNA
CC   can be inhibited by oligonucleotides of specific composition that
CC   hybridise to its translation initiation site (see AAV09215).
CC   The oligonucleotide compositions can be used for treating, particularly
CC   chronic myelogenous leukaemia (CML).
XX
SQ   Sequence   217 AA;
```

```
  Query Match             13.2%;  Score 224;  DB 19;  Length 217;
  Best Local Similarity   27.9%;  Pred. No. 3.3e-12;
  Matches   53;  Conservative   44;  Mismatches   57;  Indels   36;  Gaps    7;

Qy       7 NFDSEERSSWYWGRLSRQEAVALLQGQRH-GVFLVRDSSTSPGDYVLSVSENSRVSHYII 65
           |:   :   |::|:: | :|  :|  ||| | ||:|:| ::|||: |||   : | |: :
Db      51 nyiemkphpwffgkiprakaeemlskqrhdgafliresesapgdfslsvkfgndvqhfkv 110

Qy      66 NSSGPRPPVPPSPAQPPPGVSPSRLRIGDQEFDSLPALLEFYKIHYLDTTTLIEPVARSR 125
             |                 :  :   :|:|| |:::::     :|:    |:|::
Db     111 lrdg----------------agkyflwvvkfnslnelvdyhr-----sts----vsrnq 144

Qy     126 QGSGVILRQ-----EEAEYVRALFDFNGNDEEDLPFKKGDILRIRDKPEEQWWNAEDSEG 180
           |   : ||      ::  ||:|||||:  :: :| |::|| : : |  :  ||      |
Db     145 q---iflrdieqvpqqptyvqalfdfdpqedgelgfrrgdfihvmdnsdpnwwkga-chg 200

Qy     181 KRGMIPVPYV 190
           : || |  ||
Db     201 qtgmfprnyv 210


RESULT  11
AAR84636
ID   AAR84636 standard; Protein; 217 AA.
XX
AC   AAR84636;
XX
DT   25-FEB-1996  (first entry)
XX
DE   Grb2 protein.
XX
KW   Grb2; BCR-ABL; tyrosine kinase; transformation; Ras; oncoprotein;
KW   leukaemia.
XX
OS   Homo sapiens.
XX
FH   Key             Location/Qualifiers
FT   Domain          5..55
FT                   /label= SH3_domain
FT   Domain          60..157
FT                   /label= SH2_domain
FT   Domain          163..214
FT                   /label= SH3_domain
XX
PN   CA2113494-A.
XX
PD   15-JUL-1995.
XX
PF   14-JAN-1994;   94CA-2113494.
XX
PR   14-JAN-1994;   94CA-2113494.
XX
PA   (MOUN ) MOUNT SINAI HOSPITAL CORP.
PA   (TEXA ) UNIV TEXAS.
XX
PI   Arlinghaus R,  Gish G,  Liu J,  Pawson A,  Puíl L;
XX
DR   WPI; 1995-302931/40.
DR   N-PSDB; AAT05108.
XX
PT   Detection of agents that modify BCR-ABL mediated transformation -
PT   useful in treatment of leukaemia and other malignancies
XX
PS   Example 1; Page 48; 106pp; English.
XX
CC   The human Grb2 protein (AAR84636) acts as an adaptor to link BCR-ABL
CC   tyrosine-kinase to mSos1 (AAR84638).  The resulting BCR-ABL-Grb2-mSos1
CC   complex activates the Ras pathway leading to morphological
CC   transformation.  Substances that affect this transformation are
CC   useful in the treatment of chronic, acute myelogenous or acute
CC   lymphocytic leukaemia, and are identified by reaction with
CC   Grb2 (or its SH2 or SH3 domains) and with a cpd. contg. the Brb2-
CC   binding site on BCR-ABL, Sos or Shc and examination of any resulting
CC   complex.
XX
SQ   Sequence   217 AA;


  Query Match             13.1%;  Score 222;  DB 16;  Length 217;
  Best Local Similarity   27.4%;  Pred. No. 5e-12;
  Matches   52;  Conservative   45;  Mismatches   57;  Indels   36;  Gaps    7;

Qy       7 NFDSEERSSWYWGRLSRQEAVALLQGQRH-GVFLVRDSSTSPGDYVLSVSENSRVSHYII 65
           |:   :   |::|:: | :|  :|  ||| | |::|:| ::|||: |||   : | |: :
Db      51 nyiemkphpwffgkiprakaeemlskqrhdgafviresesapgdfslsvkfgndvqhfkv 110

Qy      66 NSSGPRPPVPPSPAQPPPGVSPSRLRIGDQEFDSLPALLEFYKIHYLDTTTLIEPVARSR 125
             |                 :  :   :|:|| |:::::     :|:    |:|::
Db     111 lrdg----------------agkyflwvvkfnslnelvdyhr-----sts----vsrnq 144

Qy     126 QGSGVILRQ-----EEAEYVRALFDFNGNDEEDLPFKKGDILRIRDKPEEQWWNAEDSEG 180
           |   : ||      ::  ||:|||||:  :: :| |::|| : : |  :  ||      |
Db     145 q---iflrdieqvpqqptyvqalfdfdpqedgelgfrrgdfihvmdnsdpnwwkga-chg 200

Qy     181 KRGMIPVPYV 190
           : || |  ||
Db     201 qtgmfpphyv 210


RESULT  12
AAR26061
ID   AAR26061 standard; Protein; 317 AA.
XX
AC   AAR26061;
XX
DT   02-FEB-1993  (first entry)
XX
DE   Growth Factor Receptor Bound protein GRB-2 partial sequence.
XX
KW   Tyrosine phophorylation; epidermal growth factor receptor; EGFR;
KW   src homology domain; SH2; SH3.
XX
OS   Homo sapiens.
XX
FH   Key             Location/Qualifiers
FT   Domain          30
FT                   /note= "start of SH2 domain"
FT   Domain          133
FT                   /note= "start of SH3 domain"
FT   Misc-difference 183
FT                   /note= "corresponds to CNG codon,
FT                    where N is unknown"
FT   Misc-difference 184
FT                   /note= "corresponds to TGA codon"
FT   Misc-difference 196
FT                   /note= "corresponds to TAA codon"
FT   Misc-difference 199
FT                   /note= "corresponds to TGA codon"
FT   Misc-difference 215
FT                   /note= "corresponds to TGA codon"
FT   Misc-difference 231
FT                   /note= "corresponds to TGA codon"
FT   Misc-difference 202
FT                   /note= "corresponds to TAA codon"
FT   Misc-difference 299
FT                   /note= "corresponds to TGA codon"
FT   Misc-difference 301
FT                   /note= "corresponds to TAA codon"
FT   Misc-difference 302
FT                   /note= "corresponds to TAA codon"
FT   Misc-difference 315
FT                   /note= "corresponds to TAG codon"
XX
PN   WO9213001-A.
XX
PD   06-AUG-1992.
```

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XX
PF   17-JAN-1992;   92WO-US00434.
XX
PR   18-JAN-1991;   91US-0643237.
XX
PA   (UYNY ) UNIV NEW YORK STATE.
XX
PI   Margolis BL,  Schlessinger J,  Skolnik EY;
XX
DR   WPI; 1992-284605/34.
DR   N-PSDB; AAQ27255.
XX
PT   Probe from tyrosine-phosphorylated portion of receptor tyrosine
PT   kinase - used for detection of proteins capable of binding to
PT   receptors, useful for e.g. identifying susceptibility to cancer
PT   and diabetes
XX
PS   Claim 18; Fig 16; 86pp; English.
XX
CC   The GRB-2 partial coding sequence was isolated from human brain stem
CC   lambda gt11 expression library by screening with tyrosine
CC   phosphorylated C-terminal tail of the EGF Receptor. The amino acid
CC   sequence deduced from the nucleotide sequence (the "ORF" includes
CC   several nonsense codons !) contains unique SH2 and SH3 domains.
CC   See also AAQ27254.
XX
SQ   Sequence   317 AA;


  Query Match             12.4%;  Score 210;  DB 13;  Length 317;
  Best Local Similarity   28.0%;  Pred. No. 9.8e-11;
  Matches   52;  Conservative   44;  Mismatches   54;  Indels   36;  Gaps    8;

Qy       7 NFDSEERSSWYWGRLSRQEAVALLQGQRH-GVFLVRDSSTSPGDYVLSVSENSRVSHYII 65
Db      21 nyiemkphpwffgkiprakaeemlskqrhdgafliresesapgdfslsvkfgtmcstfkv 80

Qy      66 NSSGPRPPVPPSPAQPPPGVSPSRLRIGDQEFDSLPALLEFYKIHYLDTTTLIEPVARSR 125
Db      81 lprwsrevlp--------------lvv---kfnslnelvdyhr-----sts----vsrnq 114

Qy     126 QGSGVILRQ-----EEAEYVRALFDFNGNDEEDLPFKKGDILRIRDKPEEQWWNAEDSEG 180
Db     115 q---iflrdieqvpqqptyvqalfdfdpqedgelgfrrgdfihvmdnsdpnwwkga-chg 170

Qy     181 KRGMIP 186
Db     171 qtgmfp 176


RESULT  13
AAR90583
ID   AAR90583 standard; Protein; 1290 AA.
XX
AC   AAR90583;
XX
DT   09-APR-1996  (first entry)
XX
DE   Phospholipase C-gamma-1.
XX
KW   Phospholipase C-gamma-1; PLC-gamma-1; phosphoinositide.
XX
OS   Rattus sp.
XX
PN   US5474921-A.
XX
PD   12-DEC-1995.
XX
PF   15-OCT-1993;   93US-0138641.
XX
PR   15-OCT-1993;   93US-0138641.
XX
PA   (MERI ) MERCK & CO INC.
XX
PI   Koblan KS,  Pompliano DL;
XX
DR   WPI; 1996-048545/05.
DR   N-PSDB; AAT12292.
XX
PT   Method for expression and isolation of mammalian phospholipase
PT   C-gamma-1 - useful for determining inhibitory activity of test
PT   compounds towards phospho:inositide-specific phospholipase-C enzyme.
XX
PS   Claim 1; Column 13-20; 25pp; English.
XX
CC   Rat phosphoinositide-specific phospholipase C-gamma-1 (EC-3.1.4.3)
CC   (AAR90583) is obtd. by expression in a transformed bacterial host of
CC   cDNA (AAT12292) encoding rat PLC-gamma-1 and DNA coding for an epitope
CC   tag (Glu-Glu-Phe) which is incorporated at the C-terminus of the
CC   recombinant PLC-gamma-1 to facilitate affinity purification.  The
CC   recombinant PLC-gamma-1 is used to assay the inhibitory activity of
CC   a test cpds. against PLC-gamma-1.
XX
SQ   Sequence   1290 AA;


  Query Match             10.5%;  Score 177;  DB 17;  Length 1290;
  Best Local Similarity   23.2%;  Pred. No. 5.5e-07;
  Matches   48;  Conservative   32;  Mismatches   85;  Indels   42;  Gaps    5;

Qy       9 DSEERSSWYWGRLSRQEAV-ALLQGQRHGVFLVRDSSTSPGDYVLSVSENSRVSHYIINS 67
Db     661 naheskewyhasltraqaehmlmrvprdgaflvr-krnepnsyaisfraegkikhcrvqq 719

Qy      68 SGPRPPVPPSPAQPPPGVSPSRLRIGDQEFDSLPALLEFY---------KIHYLDTTTLI 118
Db     720 eg-----------------qtvmlgnsefdslvdlisyyekhplyrkmklrypineeal 761

Qy     119 EPVARSRQGSGVILRQEEAEY-------------VRALFDFNGNDEEDLPFKKGDILRIR 165
Db     762 ekigtaepdygalyegrnpgfyveanpmptfkcavkalfdykaqredeltftksaiiqnv 821

Qy     166 DKPEEQWWNAEDSEGKRGMIPVPYVEK 192
Db     822 ekqdggwwrgdyggkkqlwfpsnyvee 848


RESULT  14
AAY49419
ID   AAY49419 standard; Protein; 845 AA.
XX
AC   AAY49419;
XX
DT   13-MAR-2000  (first entry)
XX
DE   PKA substrate, Vav-family protein.
XX
KW   Protein kinase A; PKA; PKA signaling pathway; phosphorylation; cancer;
KW   kinase substrate; immunosuppressive disorder; proliferative disease;
KW   HIV infection; AIDS; immunodeficiency; autoimmune disease;
KW   systemic lupus erythematosus; Vav-family.
XX
OS   Homo sapiens.
XX
PN   WO9962315-A2.
XX
PD   02-DEC-1999.
XX
PF   27-MAY-1999;   99WO-GB01680.
XX
PR   27-MAY-1998;   98NO-0002419.
PR   30-DEC-1998;   98US-0114240.
XX
PA   (LAUR-) LAURAS AS.
PA   (JONE/) JONES E L.
XX
```

PI Hansson V, Levy FO, Mustelin T, Skalhegg BS, Sundvold V, Tasken K;
PI Vang T, Altman A, Munshi A;
XX
DR WPI; 2000-086801/07.
DR N-PSDB; AAZ46490.
XX
PT Altering the activity of protein kinase signaling pathways, used for
PT treating immunosuppressive disorders, e.g. AIDS, proliferative
PT disorders, e.g. cancers or autoimmune diseases -
XX
PS Claim 17; Page 93; 111pp; English.
XX
CC The invention provides a novel method of altering the activity of the
CC protein kinase A (PKA) signaling pathway in a cell that comprises
CC altering the extent of phosphorylation of one or more PKA substrates, or
CC kinase substrates downstream in the PKA signaling pathway. Pharmaceutical
CC compositions containing a nucleic acid molecule that encodes a PKA
CC substrate, or fragment, precursor or functionally equivalent variant,
CC where the sequence is modified to alter its susceptibility to
CC phosphorylation by PKA can be used for treating a disorder exhibiting
CC abnormal PKA signaling activity, immunosuppressive disorders or
CC proliferative diseases. They can be used for treating e.g. HIV
CC infection, AIDS, common variable immunodeficiency or cancers. Conditions
CC in which upregulation of the PKA pathway is required, such as autoimmune
CC disease, e.g. systemic lupus erythematosus, may also be treated. The
CC present sequence represents a PKA substrate, wherein the substrate is in
CC the Vav-family, preferably Vav, Vav2, Vav-3, Vav-3beta, Vav transforming
CC protein and Vav-2 oncogene.
XX
SQ Sequence 845 AA;

Query Match 10.3%; Score 174; DB 21; Length 845;
Best Local Similarity 27.3%; Pred. No. 5.8e-07;
Matches 54; Conservative 27; Mismatches 67; Indels 50; Gaps 8;

```
Qy     16 WYWGRLSRQEAVALLQGQRHGVFLVRDSSTSPGDYVLSVSENSRVSHY-IINSSGPRPPV 74
           || | : |  | ::|  :  | ||||      :: :|:  |  | |  |: : |
Db    671 wyagpmeragaesilanrsdgtflvrqrvkdaaefaisikynvevkhikimtaeg----- 725

Qy     75 PPSPAQPPPGVSPSRLRIGDQE-FDSLPALLEFYK-------IHYLDTT---------- 115
                      || ::: |  |  |:|||:          ||||
Db    726 -------------lyritekkafrgltelvefyqqnslkdcfksldttlqfpfkepekr 771

Qy    116 TLIEPVARSRQGSGVILRQEEAEYVRALFDFNGNDEEDLPFKKGDILRIRDKPEEQ-WWN 174
          |:  |   | :  |          :| :||   |  :|  |:|||::| :|  :| ||
Db    772 tisrpavgstkyfgt---------akarydfcardrselslkegdiikilnkkgqqgwwr 822

Qy    175 AEDSEGKRGMIPVPYVEK 192
            |   |: |  |  |||:
Db    823 ge-iygrvgwfpanyvee 839
```

RESULT 15
AAY27125
ID AAY27125 standard; Protein; 797 AA.
XX
AC AAY27125;
XX
DT 14-SEP-1999 (first entry)
XX
DE Amino acid sequence of human Vav.
XX
KW LAT; tyrosine kinase; linker for activation of T cell; TCR; human;
KW T-cell receptor; TCR signalling pathway; neoplasia; inflammation;
KW hypersensitivity; allergy; microbial infection; genetic disease;
KW autoimmune disease; graft rejection; modulator; Vav.
XX
OS Homo sapiens.
XX
PN WO9932627-A2.
XX
PD 01-JUL-1999.
XX
PF 23-DEC-1998; 98WO-US27400.
XX
PR 23-DEC-1997; 97US-0068690.
XX
PA (USSH) US DEPT HEALTH & HUMAN SERVICES.
XX
PI Samelson LE, Zhang W;
XX
DR WPI; 1999-418926/35.
DR N-PSDB; AAX89078.
XX
PT Linker for activation of T cell protein used to, e.g. screen for
PT modulators of T cell signalling
XX
PS Disclosure; Fig 11B; 125pp; English.
XX
CC The invention relates to a protein tyrosine kinase substrate LAT (linker
CC for activation of T cells) protein. Modulation of interaction between LAT
CC and the T-cell receptor (TCR) affects the TCR signalling pathway. LAT is
CC a substrate for tyrosine kinases and becomes phosphorylated after TCR
CC engagement, resulting in recruitment of other signalling molecules. LAT
CC is used to identify and test (ant)agonists of tyrosine kinase signalling
CC pathways, i.e. modulation of interaction between tyrosine kinase
CC substrates and intracellular ligands or between these ligands and other
CC members of the pathway, including identification of downstream signalling
CC proteins, particularly in immune system cells. These modulators are
CC potentially useful as drugs and diagnostic agents, particularly for
CC diseases that involve undesirable cell proliferation, differentiation,
CC growth or T cell anergy, e.g. neoplasia, inflammation, hypersensitivity/
CC allergy, microbial infection, metabolic, genetic or autoimmune diseases,
CC graft rejection. LAT is also used to generate specific antibodies, used
CC for detection of LAT. Nucleic acid that encodes LAT, or its fragments,
CC are used to identify homologous sequences in other species; to detect the
CC LAT gene and as sources of antisense therapeutics. Modulators of LAT are
CC potentially more specific and less toxic than known immunosuppressants
CC such as cyclosporin. The present sequence represents the amino acid
CC sequence of human Vav.
XX
SQ Sequence 797 AA;

Query Match 10.2%; Score 172.5; DB 20; Length 797;
Best Local Similarity 27.1%; Pred. No. 7.3e-07;
Matches 54; Conservative 27; Mismatches 67; Indels 51; Gaps 8;

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Qy     16 WYWGRLSRQEAVALLQGQRHGVFLVRDSSTSPGDYVLSVSENSRVSH--YIINSSGPRPP 73
           || | : |  | ::|  :  | ||||       :: :|:  |  | |   |: : |
Db    622 wyagpmeragaesilanrsdgtflvrqrvkdaaefaisikynvevkhtvkimtaeg---- 677

Qy     74 VPPSPAQPPPGVSPSRLRIGDQE-FDSLPALLEFYK-------IHYLDTT---------- 115
                          || ::: |  |  |:|||:          ||||
Db    678 --------------lyritekkafrgltelvefyqqnslkdcfksldttlqfpfkepek 722

Qy    116 -TLIEPVARSRQGSGVILRQEEAEYVRALFDFNGNDEEDLPFKKGDILRIRDKPEEQ-WW 173
           |:  |   | :  |           :| :||   |  :|  |:|||::| :|  :| ||
Db    723 rtisrpavgstkyfgt---------akarydfcardrselslkegdiikilnkkgqqgww 773

Qy    174 NAEDSEGKRGMIPVPYVEK 192
             |   |: |  |  |||:
Db    774 rge-iygrvgwfpanyvee 791
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Search completed: September 27, 2001, 16:41:22
Job time: 695 sec